

REMARKS

With entry of this Amendment, claims 63-147 are pending in the application. By this Amendment, claims 63, 93, 94, 117, 118, 122, 123, 127, and 146 have been amended for clarity and to resolve non-substantive issues relating to restriction practice in the application.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Appendix. Version with Markings to Show Changes Made."

Restriction Requirement

Applicants respectfully request reconsideration of the pending Restriction Requirement, in part, on the basis that it is not directed to the currently pending claims. A Preliminary Amendment was filed in this matter on March 21, 2000 and received by the Patent Office on April 3, 2000, as evidenced by the enclosed copy of the stamped return postcard. A copy of the Preliminary Amendment as filed is attached. Formal entry and consideration of the Preliminary Amendment is respectfully requested.

The Preliminary Amendment requested that claims 1-62 be canceled without prejudice, and that claims 63-147 be added. In the Remarks presented in the Preliminary Amendment, Applicants submitted that the changes were consistent with the original Restriction Requirement mailed on December 10, 1997 in the parent application, Serial No. 08/892,403, filed July 15, 1997.

Applicants now submit herein a second Amendment to the claims prior to substantive examination, which Amendment is intended to resolve issues raised in the pending (February 9, 2001) Restriction Requirement. In this regard, the Amendment reintroduces subject matter withdrawn in the above-noted Preliminary Amendment, to clarify the claims so that they generally embrace the invention of Group V identified in the pending Restriction Requirement (i.e., "isolated RSV modified by introduction of a termination codon or in a GS or GE transcription signal, classified in class 424, subclass 211.1").

The present claims facilitate prosecution of the application by integrating many of the species identified by the Office in coordinately drafted claim series, obviating detailed redrafting of the claims upon allowance of generic subject matter corresponding to the elected invention(s). However, Applicants reserve the right to submit claims to additional species within such generic invention(s) as may be allowed by the Office within this or a related application.

The pending claims differ from the identified Group V invention at least in part by the incorporation of language directed to recombinant RSV having a "nucleotide modification to a cis-acting regulatory sequence". The following Remarks excerpted from the above-referenced Preliminary Amendment (and referring to the Restriction in the parent application) are believed to clarify that the amended claims also satisfy the pending Restriction Requirement and are generally consistent with the designation of species therein:

The present claims encompass in whole or in part subject matter identified by the Office as representing Groups VI and VIII specified in the restriction requirement in the parent application. These Groups were characterized by the Office to embrace recombinant RSV with a "modification in a termination codon or a GS or GE signal" (Group VI), and RSV with a "nucleotide modification to a cis-acting regulatory sequence" (Group VIII), respectively, as well as dependent claims related thereto. Applicants' Preliminary Amendment presented herein consolidates this subject matter \* \* \*.

In this regard, Applicants note that Group VIII identified by the Office includes claims that are generically directed to recombinant RSV having a modification of a cis-acting regulatory sequence. Group VI identified by the Office includes claims more specifically directed to RSV having a modification of a gene start (GS) or gene end (GS) signal sequence, which sequences are clearly taught in the specification and recognized in the art as examples of cis-acting regulatory sequences \* \* \*.

Thus, the claims presented above are believed to be consistent with the Restriction Requirement in the parent application. The claims now presented for consideration are clearly related in fundamental aspects. Further restriction or species segregation of these claims would impose an undue burden on Applicants and result in a protracted, uncoordinated review process. In contrast, although certain aspects of the claims may be separate and

distinct, no undue burden would be imposed on the Office to prosecute these claims together on their merits in a single application. The respective subject matter of the claims presented herein does not present "a separate subject for inventive effort, and also a separate field of search" (see, e.g., MPEP § 808.02).

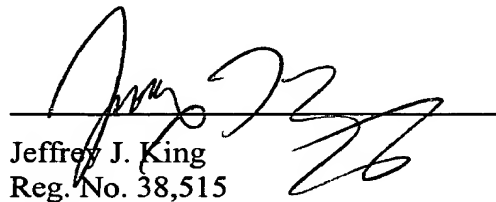
In view of the foregoing, Applicants submit that the present Amendment obviates all pending Restriction Requirements, without need to further consider the merits of any pending Restriction. Applicants further submit that, if the Office concurs with the present response to Restriction Requirement, an election of species is hereby made to the species identified as "RSV with a modification in an NS1 gene" (numbered above as species 14. See, page 4 of the February 9, 2001 Restriction Requirement) as a representative species within the invention(s). The present "elections" are made without prejudice or acquiescence to any position taken by the Office concerning the possible nature and/or existence of distinct inventions among the claims. Applicants traverse the pending Restriction and Species Election Requirement on these limited grounds and reserve the right to file a divisional or related application to the claims of non-elected groups.

Applicants believe that all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

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## APPENDIX

### VERSION WITH MARKINGS TO SHOW CHANGES MADE

#### IN THE CLAIMS:

Claims 63, 93, 94, 117, 118, 122, 123, 127, and 146 have been amended as follows:

1                   63.     (Amended) An isolated infectious recombinant respiratory syncytial  
2 virus (RSV) comprising a RSV genome or antigenome, a major nucleocapsid (N) protein, a  
3 nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a RNA polymerase  
4 elongation factor, wherein a modification is introduced within the genome or antigenome  
5 comprising a deletion, insertion, substitution, rearrangement, or nucleotide modification of a  
6 cis-acting regulatory sequence or introduction of a translation termination codon within the  
7 recombinant RSV genome or antigenome.

1                   93.     (Amended) The recombinant RSV of claim [90] 63, wherein  
2 expression of a selected RSV gene is reduced or ablated by introduction of one or more  
3 translation termination codons.

1                   94.     (Amended) The recombinant RSV of claim [90] 63, wherein  
2 expression of a selected RSV gene is reduced or ablated by introduction of multiple  
3 translation termination codons.

1                   117.    (Amended) A method for stimulating the immune system of an  
2 individual to induce protection against respiratory syncytial virus, which comprises  
3 administering to the individual an immunologically sufficient amount of the isolated  
4 attenuated recombinant RSV of claim [1] 63.

1                   118.    (Amended) The method of claim 117, wherein the recombinant virus  
2 is administered in a dose of [103 to 106] 10<sup>3</sup> to 10<sup>6</sup> PFU of the attenuated RSV.

1                   122.    (Amended) A vaccine to induce protection against RSV, which  
2 comprises an immunologically sufficient amount of the isolated attenuated recombinant RSV  
3 of claim [1] 63 in a physiologically acceptable carrier.

1                   123. (Amended) The vaccine of claim 122, formulated in a dose of [103 to  
2   106]  $10^3$  to  $10^6$  PFU of the attenuated RSV.

1                   127. (Amended) An isolated polynucleotide molecule comprising a  
2   respiratory syncytial virus (RSV) genome or antigenome which is modified by a deletion,  
3   insertion, substitution, rearrangement, or nucleotide modification of a cis-acting regulatory  
4   sequence, or by introduction of a translation termination codon.

1                   146. (Amended) A method for producing an infectious respiratory syncytial  
2   virus (RSV) particle from one or more isolated polynucleotide molecules encoding said RSV,  
3   comprising:

4                   expressing in a cell or cell-free lysate an expression vector comprising an  
5   isolated polynucleotide comprising a recombinant RSV genome or antigenome which is  
6   modified by a deletion, insertion, substitution, rearrangement, or nucleotide modification of a  
7   cis-acting regulatory sequence, or by introduction of a translation termination codon.